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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/766,857	LEWIS ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/29/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,17 and 34-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,17 and 34-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 16-17 and 34-48 are pending. Applicants previously cancelled claims 1-15 and 18-33. Applicants have amended claim 16. Receipt and consideration of Applicants' amended claim set and arguments/remarks submitted on May 29, 2008 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments and/or persuasive arguments.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/29/2008 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34-36, 38-40, 42-44, and 46-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 34-36, 38-40, 42-44, and 46-48 are internally inconsistent and thus indefinite. Claim 34-40 and 42-48 all depend either indirectly or directly from claim 16, which utilizes

closed, "consisting of" claim language to describe the claimed aerosol. However, dependent claims 34-36, 38-40, 42-44, and 46-48 utilize open, "comprising", claim language, which is broader than "consisting of". Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16-17, 35, 37, 39, 41, 43, 45, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al. (U.S. Patent No. 5,776,432) ("Schultz") in view of Radhakrishnan et al. (U.S. Patent No. 5, 192,528) (already of record).

Applicant Claims

Applicants claim an aerosol produced from a solution consisting of: (a) one or more solubilized active materials selected from a group of drugs consisting of salbutamol (i.e. albuterol), salts of salbutamol, beclomethasone dipropionate, ipratropium bromide, and combinations thereof, (b) a propellant consisting of a mixture of HFA 227 and HFA 134a in a ratio of HFA 227:HFA 134a ranging from 10:90 to 90:10, (c) ethanol, and wherein the aerosol is composed of particles which have a MMAD greater than 2 microns and a fine particle fraction of particles with a size less than 4.7 microns of at lest 40%. It is also noted that dependent claims 34-36, 38-40, 42-44, and 46-48 utilize open, "comprising" claim language, which is deemed as controlling in comparison to "consisting of" claim language of parent claim 16.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Schultz teaches pharmaceutical **solution aerosol formulations comprising (a) a therapeutically effective amount of beclomethasone dipropionate, (b) ethanol, and (c) 1,1,1,2-tetrafluoroethane (i.e. HFA 134a), 1,1,1,2,3,3,3-heptafluoropropane, and mixtures thereof, wherein the propellant preferably constitutes an amount from about 80-99% w/w,**

preferably ethanol in amounts from about 2-12% w/w, and preferably about 0.02 to about 0.6% w/w of beclomethasone dipropionate (title; abstract; col. 1, line 60 through col. 2, line 5; col. 2, lines 19-58; claims 1-6 and 9-10). Schultz teaches that the invented formulations may be utilized to treat asthma (e.g. claim 1).

Radhakrishnan teaches in Figure 1 the correlation between aerosol particle size, expressed as MMAD (col. 6, lines 55-60), and the final location of said aerosol particle in the respiratory system upon inhalation. **Deposition of aerosol particles (i.e. MMAD) in the bronchi requires particle sizes between 1.1-4.7 microns** (Figure 1). Treatment directed to the upper respiratory tract, such as the **treatment of bronchial asthma with corticosteroids (e.g. beclomethasone and beclomethasone dipropionate)**, requires **particle sizes (i.e. MMAD) ranging between about 2.1 microns and 4.7 microns.** Corticosteroids are anti-inflammatory compounds that are known for the treatment of various lung conditions, including bronchial asthma of the upper respiratory system and interstitial lung disease of the lower respiratory system (col. 2, lines 31-45; col. 4, lines 8-25; col. 7, lines 57-63; and col. 36-42). It is also noted that particle sizes ranging from 1.1 microns to 2.1 microns both are recognized as reaching the secondary bronchi upon inhalation.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Schultz is silent as to the MMAD and fine particle fraction of aerosol particles produced from the invented aerosol solution formulations. This deficiency is obviated by the teachings of Schultz and Radhakrishnan. Radhakrishnan has been provided to demonstrate that at the time of Applicants' invention the correlation between particle size, expressed as MMAD and the final

destination of inhaled particles in the respiratory tract was well known. Radhakrishnan also establishes that which particle sizes were deemed appropriate to treat different respiratory diseases was also well known at the time of Applicants' claimed invention.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been *prima facie* obvious to a person of ordinary skill at the time of the instant invention to combine the teachings of Schultz and Radhakrishnan, because Radhakrishnan provides the ordinary skilled artisan with the knowledge of particle sizes used to treat various respiratory diseases and distinguishes between particles sizes expressed as MMAD that are suitable for the treatment of upper respiratory diseases such as bronchial asthma (i.e. a particle size between about 2.1 microns and 4.7 microns). Radhakrishnan demonstrates that it was well known that treatment of bronchial asthma requires particle sizes between about 2.1 microns and 4.7 microns. Thus, an ordinary skilled artisan would be motivated to modify and/or optimize the particle size of Schultz' invented formulations, which are disclosed as being suitable for the treatment of asthma, to have a particle size in MMAD between about 2.1 microns and 4.7 microns. It would have been *prima facie* obvious to a person of ordinary skill at the time of the instant invention that the aerosol solution formulations taught and suggested by Schultz could be modified to comprise both HFA 227 and HFA 134a in a ratio from 10:90 to 90:10, because Schultz suggests that mixtures of HFA 227 and HFA 134a are suitable. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for

an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. Regarding the recited MMAD and fine particle fractions of the claimed aerosols, these properties would be exhibited by aerosols made from the formulations suggested by Schultz, because the formulations suggested by Schultz are substantially similar to those used by Applicants to obtain the claimed aerosols. Applicants' declaration is noted, but does not address or affect the merits of the instant rejection and is not further addressed herein. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments filed 29 May 2008 as applied to the new rejection have been fully considered but they are not persuasive. Applicants' traversal arguments as applied to the instant rejection are understood to be that (1) Schultz corresponds to EP 0553298, which is discussed in Applicants' specification on page 7, line 25 through page 8, line 22, and allegedly teaches aerosol solution formulations that form particles with an MMAD of 1.1 microns upon actuation from a metered dose inhaler, as allegedly evidenced by Leach; and (2) there is allegedly nothing present in Schultz or commonly known in the prior art at the time of Applicants' invention that would have taught, suggested, or motivated the ordinary skilled artisan to obtain aerosols characterized by MMAD of greater than 2 microns.

The Examiner respectfully disagrees with Applicants' traversal arguments. Regarding (1), Applicants have not established the equivalency of Schultz and EP 0553298. Furthermore, it is noted that Applicants' description of EP 0553298 in their specification makes no reference or commentary concerning the MMAD of the beclomethasone dipropionate aerosol solution formulations disclosed therein. Thus, Applicants' specification description of EP 0553298 does not provide any evidence supporting the allegation that the formulations of EP 0553298 have an MMAD of 1.1 microns or that Schultz is equivalent to EP 0553298. It is further noted that Applicants have not presented any objective data supporting their assertion that Schultz' aerosol formulations necessarily have a MMAD of 1.1 microns. Absent evidence supporting Applicants' assertions regarding the MMAD of Schultz' aerosol particles, this is mere argument. Attorney argument in the absence of objective evidence is unpersuasive. Concerning the Leach reference, Exhibit A is not present with Applicants' remarks (i.e. the Leach reference has not been submitted); thus, the Examiner is unable to consider the alleged evidence in Leach at this time. If Applicants would like the Leach reference considered with their remarks, they are kindly requested to provide the Office with a copy of Leach and to cite said reference on an IDS to make this reference of record.

Regarding (2), the prior art clearly recognized that particle sizes expressed in MMAD suitable for the treatment of bronchial asthma (Radhakrishnan) necessarily must be in a range between about 2.1 microns and 4.7 microns. Schultz' invented compositions are disclosed as having utility for the treatment of asthma. Thus, an ordinary skilled artisan utilizing Schultz' invented compositions to treat bronchial asthma would clearly be motivated to modify and/or optimize the MMAD of the aerosol particles of Schultz' invented composition to be with the

range of about 2.1 microns and 4.7 microns. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Claims 34, 36, 38, 40, 42, 46, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al. (U.S. Patent No. 5,776,432) ("Schultz") in view of Radhakrishnan et al. (U.S. Patent No. 5, 192,528) as applied to claims 16-17, 35, 37, 39, 41, 43, 45, and 47 above, and further in view of Stefely et al. (U.S. Patent No. 6,126,919).

Applicant Claims

Applicants claim an aerosol produced from a solution as described above in the instant office action wherein the aerosol comprises as the active material, salbutamol (i.e. albuterol), salts of salbutamol, ipratropium bromide, or combinations thereof.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Schultz and Radhakrishnan were set forth above in the instant office action. Stefely teaches preferred pharmaceutical formulations designed for oral/nasal inhalation, wherein the formulation comprises a drug suitable for the treatment of diseases such as asthma, COPD, etc., wherein preferred drugs include **albuterol (i.e. salbutamol), beclomethasone dipropionate, budesonide, ipratropium bromide, salts, solvates, and mixtures thereof and the formulation is preferably in the form of a solution** (col. 8, lines 40-42, 59-62; col. 9, lines 3-6 and 16-37; and claims 1-3). The formulations may be contained within a metered dose

inhaler and also may comprise a mixture of hydrofluorocarbon propellants, selected from **HFA 134a and HFA 227** (claims 1-3). Stefely also teaches that suitable cosolvents include ethanol (i.e. an alcohol), isopropanol (i.e. an alcohol), acetone, etc. (e.g. claim 30 of Stefely).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Schultz is silent as to the MMAD and fine particle fraction of aerosol particles produced from the invented aerosol solution formulations and lacks the teaching of aerosols made from HFA aerosol solution formulations wherein the active material is salbutamol (i.e. albuterol), salts of salbutamol, ipratropium bromide, or combinations thereof. These deficiencies are obviated by the teachings of Schultz and/or Stefely.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been *prima facie* obvious to a person of ordinary skill at the time of the instant invention that the aerosol solution formulations of Schultz could be modified to comprise in addition to or in lieu of beclomethasone dipropionate other drugs known as being suitable for the treatment of asthma, such as albuterol, ipratropium bromide, and salts, solvates, and mixtures thereof. An ordinary skilled artisan would have been motivated to add albuterol, ipratropium bromide, or salts thereof to Schultz' invented formulations or substitute beclomethasone dipropionate for one of these drugs, because albuterol, ipratropium bromide, or salts are art-recognized as being suitable for the treatment of asthma. Furthermore, an ordinary skilled artisan would have also been motivated to modify the teachings of Schultz with the teachings of

Stefely concerning the active material, because both references are in the same field of endeavor, namely aerosol solution formulations for the treatment of asthma. An ordinary skilled artisan would have had a reasonable expectation of success upon combination because Schultz and Stefely are in the same field of endeavor, and teach similar HFA propellant based aerosol solution formulations. Regarding the recited MMAD and fine particle fractions of the claimed aerosols, these properties would be exhibited by aerosols made from the formulations suggested by Schultz, because the formulations suggested by Schultz as modified with the one or more of the preferred drugs taught by Stefely are substantially similar to those used by Applicants to obtain the claimed aerosols. Applicants' declaration is noted, but does not address or affect the merits of the instant rejection and is not further addressed herein. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments filed 29 May 2008 as applied to the new rejection have been fully considered but they are not persuasive. Applicants' traversal arguments as applied to the instant rejection are the same arguments rebutted above in the previous rejection under 35 USC §103(a). The Office's rebuttal of these traversal arguments is herein incorporated by reference. The instant rejection is deemed to be proper.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16-17 and 34-48 (all pending claims) are rejected on the ground of nonstatutory obviousness-type double patenting of as being unpatentable over claims 1-12, 14, and 16-29 of U.S. Patent No. 6,713,047 (USPN '047) in view Stefely et al. (U.S. Patent No. 6,126,919) (USPN '919).

Independent claim 16 of the instant application has been described above in the instant office action. Independent claim 1 of USPN '047 claims a hydrofluorocarbon-based solution formulation comprising essentially the same components as the formulation utilized to product Applicants' claimed aerosol, wherein the active material is selected from an anticholinergic drug, a corticosteroid, or a beta-2 agonist. Claim 6 of USPN '047 specifies that the cosolvent is an alcohol (e.g. ethanol). The difference between the claims of USPN '047 and the instant application is that the claims of USPN '047 do not recite a specific corticosteroid (e.g.

beclomethasone dipropionate), beta-2 agonist (e.g. salbutamol), or an anticholinergic (i.e. ipratropium bromide). This deficiency is cured by the teachings of USPN '919 set forth above, which demonstrates that salbutamol (i.e. albuterol), beclomethasone dipropionate, and ipratropium bromide were known drugs at the time of Applicants' invention and would have been readily recognized by an ordinary skilled artisan as belonging to the genus of corticosteroid (i.e. beclomethasone dipropionate), beta-2 agonist (i.e. salbutamol), and anticholinergic agent (i.e. ipratropium bromide). Furthermore, USPN '919 establishes that the specific drugs (e.g. salbutamol, ipratropium bromide, and BDP) were known to have utility in the treatment of the same diseases (e.g. asthma) when used alone or in combination. USPN '919 also establishes that ethanol was a well-known and conventional alcohol cosolvent used in inhalation formulations.

Regarding the recited MMAD and fine particle fractions of the claimed aerosols, these properties would be exhibited by aerosols made from the formulations claimed by USPN 047, because these formulations as modified with the one or more of the preferred drugs taught by Stefely are substantially similar to those used by Applicants to obtain the claimed aerosols. Furthermore, as evidenced by claim 10 of USPN '047, formation of aerosol particles upon actuation of an aerosol device containing a composition, such as the one described in claim 1 of USPN '047, necessarily yields aerosol particles with a MMAD greater than 2 microns. See also claims 10-12 and 15-20, where it is clear that the compositions recited in claims 1-9 of USPN '047 were designed to generate aerosols having MMADs greater than 2 microns. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 16-17 and 34-38 (all pending claims) *prima facie* obvious over claims of claims 1-12, 14, and

16-29 of U.S. Patent No. 6,713,047 (USPN '047) in view of Stefely et al. (U.S. Patent No. 6,126,919) (USPN '919).

Response to Arguments

Applicant's arguments filed 5/29/08 have been fully considered but they are not persuasive. Applicants have traversed the instant rejection by arguing that the composition claims of USPN '047 are deficient because said claims do not recite that the claimed compositions, aerosol inhaler, or delivery system of USPN '047 is suggestive of Applicants' claimed aerosols having a MMAD greater than 2 microns.

The Examiner respectfully disagrees with Applicants' traversal argument, because the composition claimed in USPN '047 as modified by Stefely contains the same dissolved active agents, the same HFA propellants in the same ratio, and cosolvent. Furthermore, the compositions of USPN '047 necessarily generate aerosol particles having a MMAD greater than 2 microns upon delivery from an inhalation device, such as an aerosol (see for example, claims 17 and 20 of USPN '047). The instant rejection remains proper.

Claims 34-48 are rejected on the ground of nonstatutory obviousness-type double patenting of as being unpatentable over claims 1-4, 15, and 17 of U.S. Patent No. 6,716,414 (USPN '414) in view of Schultz et al. (U.S. Patent No. 5,776,432) ("Schultz") and Radhakrishnan et al. (U.S. Patent No. 5, 192,528).

Independent claim 16 of the instant application has been described above in the instant office action. The rejected dependent claims 34-36, 38-40, 42-44, and 46-48 of the instant

application utilize "comprising" claim language, thus broadening the "consisting of" language of claims 16-17 of the instant application. Independent claim 1 of USPN '414 claims a hydrofluorocarbon-based solution formulation comprising (i) formoterol, (ii) a liquefied HFA propellant, (iii) cosolvents selected from pharmaceutically acceptable alcohols (e.g. ethanol), and (iv) a mineral acid. Dependent claims 2-4 of USPN '414 indicate that the formulations comprise a steroid (e.g. beclomethasone dipropionate) or an anticholinergic (e.g. ipratropium bromide). Dependent claim 15 of USPN '414 indicates that the propellant comprises one or more HFAs selected from the group consisting of HFA 134a and HFA 227. Dependent claim 17 of USPN '414 indicates that the co-solvent comprises ethanol.

Regarding the recited MMAD and fine particle fractions of the claimed aerosols, these properties would be exhibited by aerosols made from the formulations claimed by USPN '414, because these formulations as modified with the one or more of the preferred drugs recited in claims 2-4 of USPN '414 are substantially similar to those used by Applicants to obtain the claimed aerosols. Furthermore, Schultz and Radhakrishnan establish that formulations comprising corticosteroids (e.g. beclomethasone) are art-recognized as being suitable for the treatment of asthma. The art recognizes that the treatment of bronchial asthma requires a MMAD between about 2.1 microns and 4.7 microns. Thus, even if the claimed formulations of '414 do not explicitly recite the required MMAD of Applicants' claims and an ordinary skilled artisan would have been motivated to obtain aerosol particles having a MMAD of greater than 2, 3, or 4 microns to treat bronchial asthma with a reasonable expectation of success. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 34-38 *prima facie* obvious over claims 1-4, 15, and 17 of U.S. Patent No. 6,716,414 (USPN

'414) in view of Schultz et al. (U.S. Patent No. 5,776,432) ("Schultz") and Radhakrishnan et al. (U.S. Patent No. 5, 192,528).

Response to Arguments

Applicant's arguments filed 5/29/08 have been fully considered but they are not persuasive. Applicants have traversed the instant rejection by arguing that the composition claims of USPN '414 are deficient because said claims do not recite that the claimed compositions, aerosol inhaler, or delivery system of USPN '414 is suggestive of Applicants' claimed aerosols having a MMAD greater than 2 microns.

The Examiner respectfully disagrees with Applicants' traversal argument, because the composition claimed in USPN '414 as modified by Stefely contains the same dissolved active agents, the same HFA propellants, and cosolvent. Furthermore, Schultz and Radhakrishnan establish that formulations comprising corticosteroids (e.g. beclomethasone) are art-recognized as being suitable for the treatment of asthma. The art recognizes that the treatment of bronchial asthma requires a MMAD between about 2.1 microns and 4.7 microns. Thus, even if the claimed formulations of '414 do not explicitly recite the required MMAD of Applicants' claims and an ordinary skilled artisan would have been motivated to obtain aerosol particles having a MMAD of greater than 2, 3, or 4 microns to treat bronchial asthma with a reasonable expectation of success. The instant rejection remains proper.

Claims 34-48 are rejected on the ground of nonstatutory obviousness-type double patenting of as being unpatentable over claims 1-6, 10, and 22-24 of U.S. Patent No.

6,964,759 (USPN '759) in view of Stefely et al. (U.S. Patent No. 6,126,919) (USPN '919 and Radhakrishnan et al. (U.S. Patent No. 5, 192,528).

Independent claim 16 of the instant application has been described above in the instant office action. The rejected dependent claims 34-36, 38-40, 42-44, and 46-48 of the instant application utilize "comprising" claim language, thus broadening the "consisting of" language of claims 16-17 of the instant application. Independent claim 1 of USPN '759 claims a hydrofluorocarbon-based solution formulation comprising (i) at least one solubilized quaternary ammonium compound (e.g. ipratropium bromide), (ii) at least one hydrofluorocarbon propellant, (iii) 15 % w/w or less of a cosolvent, and (iv) at least one low volatility component. The difference between the claims of USPN '759 and the instant application is that the claims of USPN '759 do not recite that the formulations may comprise beclomethasone dipropionate, salbutamol or salts of salbutamol and the formulations of USPN '759 may also comprise a low volatility component. This deficiency is cured by the teachings of USPN '919 set forth above, which demonstrates that salbutamol (i.e. albuterol), beclomethasone dipropionate, and ipratropium bromide were known drugs at the time of Applicants' invention and would have been readily recognized by an ordinary skilled artisan as belonging to the genus of corticosteroid (i.e. beclomethasone dipropionate), beta-2 agonist (i.e. salbutamol), and anticholinergic agent (i.e. ipratropium bromide).

Regarding the recited MMAD and fine particle fractions of the claimed aerosols, these properties would be exhibited by aerosols made from the formulations claimed by USPN '759, because these formulations as modified with the one or more of the preferred drugs taught by Stefely are substantially similar to those used by Applicants to obtain the claimed aerosols. It is

also noted that dependent claim 22 of USPN '759, establishes that the aerosol compositions of USPN '759 generate aerosol particles upon actuation from an inhaler having particle sizes less than 4.7 microns. Furthermore, Radhakrishnan establishes that formulations comprising corticosteroids (e.g. beclomethasone) are art-recognized as being suitable for the treatment of asthma. The art recognizes that the treatment of bronchial asthma requires a MMAD between about 2.1 microns and 4.7 microns. Thus, even if the claimed formulations of USPN '759 do not explicitly recite the required MMAD of Applicants' claims, an ordinary skilled artisan would have been motivated to obtain aerosol particles having a MMAD of greater than 2, 3, or 4 microns, but below 4.7 microns to treat bronchial asthma with a reasonable expectation of success. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 34-38 *prima facie* obvious over claims of claims 1-6, 10, and 22-24 of U.S. Patent No. 6,964,759 (USPN '759) in view of Stefely et al. (U.S. Patent No. 6,126,919) (USPN '919) and Radhakrishnan et al. (U.S. Patent No. 5, 192,528).

Response to Arguments

Applicant's arguments filed 5/29/08 have been fully considered but they are not persuasive. Applicants have traversed the instant rejection by arguing that the composition claims of USPN '759 are deficient because said claims do not recite that the claimed compositions, aerosol inhaler, or delivery system of USPN '759 is suggestive of Applicants' claimed aerosols having a MMAD greater than 2 microns.

The Examiner respectfully disagrees with Applicants' traversal argument, because the composition claimed in USPN '759 as modified by Stefely contains the same dissolved active

agents, the same HFA propellants, and cosolvent. Furthermore, Schultz and Radhakrishnan establish that formulations comprising corticosteroids (e.g. beclomethasone) are art-recognized as being suitable for the treatment of asthma. The art recognizes that the treatment of bronchial asthma requires a MMAD between about 2.1 microns and 4.7 microns. Thus, even if the claimed formulations of USPN '759 do not explicitly recite the required MMAD of Applicants' claims and an ordinary skilled artisan would have been motivated to obtain aerosol particles having a MMAD of greater than 2, 3, or 4 microns to treat bronchial asthma with a reasonable expectation of success. The instant rejection remains proper.

Claims 16-17 and 34-48 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 and 11-18 of U.S. Patent No. 7,223,381 (USPN '381) in view of Stefely et al. (U.S. Patent No. 6,126,919) (USPN '919 and Radhakrishnan et al. (U.S. Patent No. 5, 192,528).

Independent claim 16 of the instant application has been described above in the instant office action. The rejected dependent claims 34-36, 38-40, 42-44, and 46-48 of the instant application utilize "comprising" claim language, thus broadening the "consisting of" language of claims 16-17 of the instant application. Independent claim 1 of USPN '381 claims a pressurized metered dose inhaler (pMDI) containing a solution comprising (i) budesonide (a corticosteroid), (ii) a hydrofluorocarbon (HFC) propellant, and (iii) a cosolvent. Independent claims 11 and 15 of USPN '381 claim the same solution aerosol formulations present in the claimed pMDI of USPN '381. Dependent claims 4, 8, 14, and 18 of USPN '381 specify that the HFC propellant is

selected from the group consisting of HFA 227 and HFA 134a. Dependent claims 2-3, 6-7, 12-13, and 16-17 of USPN '381 specify that the cosolvent is ethanol.

A primary difference between the cited claims of USPN '381 and the rejected claims of the instant application is that the claims of USPN '381 claim a pMDI and a solution aerosol formulation, but do not claim an aerosol. It is the Examiner's position that the claimed pMDI and claimed solution aerosol formulation of USPN '381 would necessarily produce the claimed aerosol of the instant application; because both the pMDI and solution aerosol formulation of USPN '381 comprise similar components and pMDI's are art recognized devices for the production of aerosols.

One difference between the instant claims and the cited claims of USPN '381 is that the claims of USPN '199 do not recite a specific ratio of HFA 227 and HFA 134a or explicitly recite the mixture of HFA 227 and HFA 134a. It would have been prima facie obvious to combine HFA 227 and HFA 134a, because both are known HFC propellants known to be suitable in obtaining solution aerosol formulations of corticosteroids (e.g. beclomethasone and budesonide), anticholinergics (e.g. ipratropium bromide), and beta2-agonists (e.g. salbutamol) (see teachings of Stefely set forth above). Concerning the amount of HFA 227 and HFA 134a and the relative proportion of each, the recitation of mixtures thereof in the claims of USPN '381 implies all possible ratios. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some

demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. Upon optimization of the amounts of HFA 227 and HFA 134a, the relative ratio of these two propellants would necessarily be optimized as well.

Another difference between the claims of USPN '381 and the instant application is that the claims of USPN '381 do not recite beclomethasone dipropionate as the corticosteroid or that the solution aerosol formulations comprise ipratropium bromide or salbutamol. This deficiency is cured by the teachings of USPN '919 set forth above, which demonstrates that salbutamol (i.e. albuterol), beclomethasone dipropionate, and ipratropium bromide were known drugs at the time of Applicants' invention for the treatment of asthma and would have been readily recognized by an ordinary skilled artisan as belonging to the genus of corticosteroid (i.e. beclomethasone dipropionate [BDP]), beta-2 agonist (i.e. salbutamol), and anticholinergic agent (i.e. ipratropium bromide). Furthermore, USPN '919 establishes that the specific drugs (e.g. salbutamol, ipratropium bromide, and BDP) were known to have utility in the treatment of the same diseases (e.g. asthma) when used alone or in combination. USPN '919 also establishes that ethanol was a well-known and conventional alcohol cosolvent used in inhalation formulations.

Another difference between the claims of USPN '381 and the rejected claims of the instant application is that the claims of USPN '381 are silent as to the MMAD of aerosols produced upon actuation of the claimed pMDI of USPN '381 containing the aerosol formulation described supra. This deficiency is cured by the teachings of Radhakrishnan set forth above. The art recognizes that the treatment of bronchial asthma requires a MMAD between about 2.1 microns and 4.7 microns (Radhakrishnan). Thus, even if the claimed formulations of USPN

'759 do not explicitly recite the required MMAD of Applicants' claims and an ordinary skilled artisan would have been motivated to obtain aerosol particles having a MMAD of greater than 2, 3, or 4 microns to treat bronchial asthma with a reasonable expectation of success. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 16-17 and 34-48 *prima facie* obvious over claims 1-11 and 11-18 of U.S. Patent No. 7,223,381 (USPN '381) in view of Stefely et al. (U.S. Patent No. 6,126,919) (USPN '919 and Radhakrishnan et al. (U.S. Patent No. 5, 192,528).

Claims 16-17 and 34-48 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11, 21-22, 29, and 32 of U.S. Patent No. 7,347,199 (USPN '199) in view of Stefely et al. (U.S. Patent No. 6,126,919) (USPN '919 and Radhakrishnan et al. (U.S. Patent No. 5, 192,528).

Independent claim 16 of the instant application has been described above in the instant office action. The rejected dependent claims 34-36, 38-40, 42-44, and 46-48 of the instant application utilize "comprising" claim language, thus broadening the "consisting of" language of claims 16-17 of the instant application. Independent claim 1 of USPN '381 claims a pressurized metered dose inhaler (pMDI) containing a solution comprising (i) an active agent (e.g. corticosteroid, beta-adrenergic agonist, or ipratropium bromide), (ii) a hydrofluorocarbon (HFC) propellant, and (iii) a cosolvent. Claims 4-6, 9-11, 21, 29, and 32 of USPN '199 indicate that the active agent may be, for example, ipratropium bromide, salbutamol, or a corticoid steroid, such as budesonide. Claims 7, 9, and 21 of USPN '199 specify that the cosolvent is ethanol. Claims

8-9 of USPN '381 specify that the HFC propellant is selected from the group consisting of HFA 227, HFA 134a and mixtures thereof.

A primary difference between the cited claims of USPN '199 and the rejected claims of the instant application is that the claims of USPN '199claim a pMDI containing a solution aerosol formulation, but do not claim an aerosol. It is the Examiner's position that the claimed pMDI containing the solution aerosol formulation of USPN '199 would necessarily produce the claimed aerosol of the instant application; because the solution aerosol formulation contained in the pMDI's USPN '199 comprise similar components as Applicants' claimed aerosol and pMDI's are art recognized devices for the production of aerosols.

One difference between the instant claims and the cited claims of USPN '199 is that the claims of USPN '199 do not recite a specific ratio of HFA 227 and HFA 134a. Concerning the amount of HFA 227 and HFA 134a and the relative proportion of each, the recitation of mixtures thereof in the claims of USPN '199 implies all possible ratios. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. Upon optimization of the amounts of HFA 227 and HFA 134a, the relative ratio of these two propellants would necessarily be optimized as well.

Another difference between the claims of USPN '199 and the instant application is that the claims of USPN '381 do not recite beclomethasone dipropionate as the corticosteroid or that the solution aerosol formulations comprise ipratropium bromide or salbutamol. This deficiency is cured by the teachings of USPN '919 set forth above, which demonstrates that salbutamol (i.e. albuterol), beclomethasone dipropionate, and ipratropium bromide were known drugs at the time of Applicants' invention for the treatment of asthma and would have been readily recognized by an ordinary skilled artisan as belonging to the genus of corticosteroid (i.e. beclomethasone dipropionate [BDP]), beta-2 agonist (i.e. salbutamol), and anticholinergic agent (i.e. ipratropium bromide). Furthermore, USPN '919 establishes that the specific drugs (e.g. salbutamol, ipratropium bromide, and BDP) were known to have utility in the treatment of the same diseases (e.g. asthma) when used alone or in combination. USPN '919 also establishes that ethanol was a well-known and conventional alcohol cosolvent used in inhalation formulations.

Another difference between the claims of USPN '199 and the rejected claims of the instant application is that the claims of USPN '199 are silent as to the MMAD of aerosols produced upon actuation of the claimed pMDI of USPN '199 containing the aerosol formulation described supra. This deficiency is cured by the teachings of Radhakrishnan set forth above. The art recognizes that the treatment of bronchial asthma requires a MMAD between about 2.1 microns and 4.7 microns (Radhakrishnan). Thus, even if the claimed formulations of USPN '759 do not explicitly recite the required MMAD of Applicants' claims and an ordinary skilled artisan would have been motivated to obtain aerosol particles having a MMAD of greater than 2, 3, or 4 microns to treat bronchial asthma with a reasonable expectation of success. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims

16-17 and 34-48 *prima facie* obvious over claims 1-11, 21-22, 29, and 32 of U.S. Patent No. 7,347,199 (USPN '199) in view of Stefely et al. (U.S. Patent No. 6,126,919) (USPN '919 and Radhakrishnan et al. (U.S. Patent No. 5, 192,528).

Response to Arguments

Applicant's arguments filed 5/29/2008 have been fully considered but they are not persuasive. Applicants have traversed the instant rejection because none of the claims recite the claimed MMAD.

This traversal argument is unpersuasive, because the ordinary skilled artisan would have been motivated to modify and/or optimize the MMAD of the aerosols obtained from the actuation of the claimed pMDI of USPN '199 to obtain aerosol particles having a MMAD between about 2.1 microns and 4.7 microns to effectively treat bronchial asthma. Furthermore, due to the similarity in the composition of Applicants' claimed aerosol and the aerosol solution formulation contained in the claimed pMDI of USPN '199, there is a reasonable expectation that aerosols produced upon actuation of the USPN '199 claimed pMDI would necessarily exhibit similar MMAD and FPF properties. Thus, the instant rejection is considered to remain proper.

Claims 34-36, 38-40, 42-44, and 46-48 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 24-25 and 33-41 of copending application 10/435,032 (copending '032) for the reasons of record (see office action mailed 1/18/06) and restated below.

Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims have the same or similar limitations and are therefore obvious over one another. Both claim sets contain compositions comprising active materials, cosolvent, and one or more hydrofluoroalkane propellant claimed alone. Concerning the amount of different HFA propellants in the compositions of copending '032, the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. Regarding the recited MMAD and fine particle fractions of the claimed aerosols, these properties would be exhibited by aerosols made from the formulations claimed by copending '032, as evidence by dependent claims 37 and 41 which explicitly state that the formulations of claims 24-25 do not have a MMAD less than 2 microns. The rejected claims do not prohibit the inclusion of glycerol.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed 5/29/2008 have been fully considered but they are not persuasive. Applicants have not traversed the instant rejection and have requested that this rejection be held in abeyance. This rejection is maintained.

Claims 34-36, 38-40, 42-44, and 46-48 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 24, 26, 29-30, 33-36, 40-41, 44-49, and 52 of copending application 10/435,354 (copending '354) for the reasons of record (see office action mailed 1/18/06) and restated below.

Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims have the same or similar limitations and are therefore obvious over one another. Both claim sets contain compositions comprising active materials, cosolvent, low volatility components, and hydrofluoroalkane propellant claimed alone, contained within inhalers, or produced by inhalers. Concerning the amount of different HFA propellants in the compositions of copending '354, the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention. Regarding the recited MMAD and fine particle fractions of the claimed aerosols, these properties would be

exhibited by aerosols made from the formulations claimed by copending '354, as evidence by dependent claim 52, which explicitly state that the formulations of claims 24 and 40 do not have a MMAD less than 2 microns. The rejected claims do not prohibit the inclusion of glycerol. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 34-48 *prima facie* obvious over claims 24, 26, 29-30, 33-36, 40-41, 44-49, and 52 of copending application 10/435,354 (copending '354).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed 5/29/2008 have been fully considered but they are not persuasive. Applicants have not traversed the instant rejection and have requested that this rejection be held in abeyance. This rejection is maintained.

Claims 35-36, 39-40, 43-44, and 47-48 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6-7, 9, 11-17, 19-20, 22, and 24-26 of copending application 11/408,026 (copending '026) in view of Stefely et al. (U.S. Patent No. 6,126,919) (USPN '919) and Radhakrishnan et al. (U.S. Patent No. 5, 192,528).

Independent claim 16 and dependent claims 35-36, 39-40, 43-44, and 47-48 have been described supra. Independent claim 1 of copending '026 claims a method of delivering a combination of two or more active drug substances in the form of a solution by actuation of a

pressurized metered dose inhaler (pMDI). The composition administered by the method of copending '026 also comprises one or more cosolvents (e.g. ethanol) and an HFA propellant. Independent claim 14 of copending '026 claims a pMDI containing the same formulation administered in the claimed method of claim 1 of copending '026. Dependent claims 11 and 24 of copending '026 indicate that the HFA propellant is HFA 134a, HFA 227, and mixtures thereof. The primary differences between the claims of the instant application and those of copending '026 are that (1) the claims of copending '026 are drawn to different statutory subject matter (i.e. a method and a device), (2) the claims of copending '026 are silent as to the MMAD of aerosols produced by practicing the claimed method or using the claimed device of copending '026; and (3) the independent claims of copending '026 do not explicitly recite a mixture of HFA 134a and HFA 227 in any particular ratio.

Regarding the first difference, it is the Examiner's position that the practice of the claimed method using the claimed pMDI of copending '026 would necessarily product the claimed aerosol of the instant application; because both the pMDI and method of copending '026 are indicated as producing liquid droplets (i.e. liquid aerosol) upon actuation. Regarding (3), the claims of copending '026 utilize open comprising claim language, which does not exclude the use of two or more HFA propellants. Furthermore, as evidenced by dependent claim 11 and 24 of copending '026, the claimed method and pMDI of copending '026 were contemplated to contain a propellant comprising a mixture of HFA 134a and HFA 227. Concerning the amount of different HFA propellants in the compositions of copending '026, the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would

be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention.

Regarding the recited MMAD and fine particle fractions of the claimed aerosols, this deficiency is cured by the teachings of Radhakrishnan set forth above. The art recognizes that the treatment of bronchial asthma requires a MMAD between about 2.1 microns and 4.7 microns (Radhakrishnan). Thus, even if the claimed formulations of copending '026 do not explicitly recite the required MMAD of Applicants' claims and an ordinary skilled artisan would have been motivated to obtain aerosol particles having a MMAD of greater than 2, 3, or 4 microns to treat bronchial asthma with a reasonable expectation of success. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 34-36, 38-40, 42-44, and 46-48 *prima facie* obvious over claims 1-4, 6-7, 9, 11-17, 19-20, 22, and 24-26 of copending application 11/408,026 (copending '026) in view of Radhakrishnan et al. (U.S. Patent No. 5, 192,528).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 34-36, 38-40, 42-44, and 46-48 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of copending

application 12/023,315 (copending '315) in view of Stefely et al. (U.S. Patent No. 6,126,919) (USPN '919) and Radhakrishnan et al. (U.S. Patent No. 5, 192,528).

Independent claim 16 and dependent claims 35-36, 39-40, 43-44, and 47-48 have been described supra. Independent claim 1 of copending '315 claims a pressurized metered dose inhaler (pMDI) containing a pressurized solution aerosol formulation comprising (i) ipratropium bromide, (ii) a hydrofluoroalkane propellant, and (iii) at least one cosolvent. Dependent claim 4 of copending '315 indicates that the HFA propellant is HFA 134a, HFA 227, and mixtures thereof. Dependent claim 3 of copending '315 indicates that the cosolvent is ethanol. The primary differences between the claims of the instant application and those of copending '315 are that (1) the claims of copending '315 are drawn to different statutory subject matter (i.e. a pMDI), (2) the claims of copending '315 are silent as to the MMAD of aerosols produced by actuation of the claimed pMDI of copending '315; (3) the independent claim of copending '315 does not explicitly recite a mixture of HFA 134a and HFA 227 in any particular ratio; and (4) the claims of copending '315 do not recite the presence of salbutamol or a beclomethasone dipropionate.

Regarding the first difference, it is the Examiner's position that actuation of the claimed pMDI of copending '315 would necessarily produce the claimed aerosol of the instant application; because the pMDI of copending '315 contains a solution comprising the same required components as the rejected claims (e.g. dissolved ipratropium bromide, HFA propellant, and cosolvent, such as ethanol).

Regarding (3), the claims of copending '315 utilize open comprising claim language, which does not exclude the use of two or more HFA propellants. Furthermore, as evidenced by

dependent claim 4 of copending '315, the claimed pMDI of copending '315 was contemplated to contain a propellant comprising a mixture of HFA 134a and HFA 227. Concerning the amount of different HFA propellants in the compositions contained in the claimed pMDI of copending '315, the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention.

Another difference between the cited claims of copending '026 and the instant application is that the claims of copending '026 do not indicate the presence of a corticosteroid, such as beclomethasone dipropionate (BDP). This deficiency is cured by the teachings of Stefely, which sets forth that it was art-recognized that BDP, ipratropium bromide, and salbutamol were suitable for the treatment of asthma and other respiratory diseases. Because BDP, ipratropium bromide, and salbutamol were all art-recognized as having the same utility it would have been prima facie obvious to include these in the same composition contained within the claimed pMDI of copending '315. An ordinary skilled artisan would have had a reasonable expectation of obtaining an aerosol comprising one or more of BDP, ipratropium bromide, and salbutamol in solution comprising HFA propellant and ethanol, because it was art-recognized that these specific active agents formed ethanolic solutions in HFA 227, HFA 134a, and mixtures thereof.

Regarding the recited MMAD and fine particle fractions of the claimed aerosols, this deficiency is cured by the teachings of Radhakrishnan set forth above. The art recognizes that the treatment of bronchial asthma requires a MMAD between about 2.1 microns and 4.7 microns (Radhakrishnan). Thus, even if the claimed formulations of copending '026 do not explicitly recite the required MMAD of Applicants' claims and an ordinary skilled artisan would have been motivated to obtain aerosol particles having a MMAD of greater than 2, 3, or 4 microns to treat bronchial asthma with a reasonable expectation of success. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 34-36, 38-40, 42-44, and 46-48 *prima facie* obvious over claims 1-4 of copending application 12/023,315 (copending '315) in view of Stefely et al. (U.S. Patent No. 6,126,919) (USPN '919) and Radhakrishnan et al. (U.S. Patent No. 5, 192,528).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The below list of copending U.S. patent applications have been found to claim substantially similar subject matter per the obviousness-type double patenting rejections made above in the instant office action. It is incumbent upon Applicant to review this list and file terminal disclaimers as appropriate.

Application or US Patent No.

1. 10/290,225 2. 11/060,564

Conclusion

Claims 16-17 and 34-48 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/James H Alstrum-Acevedo/
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